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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,610	02/12/2004	Tsuyoshi Habe	Q79758	3941

23373 7590 10/20/2006

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,610	HABE ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Applicant's claim for benefit of 60/447,299 filed 02/14/2003 (domestic priority) under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

2. Acknowledgement is made of applicant's submitting of the information disclosure statement (IDS) on July 12, 2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement (IDS) has been considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating ocular hypertension and glaucoma with 15-keto- prostaglandin compound represented by the formula (I) wherein L, M and N are hydrogen atom, hydroxy and oxo, does not reasonably provide enablement for treating ocular hypertension and glaucoma with "15-keto-prostaglandin compound having a ring structure at the end of the ω chain" or "15 keto-prostaglandin compound represented by the formula (I)". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention relates to a method of treating ocular hypertension and glaucoma comprising administering an effective amount of 15-keto-prostaglandin compound having a ring structure at the end of the ω chain to the eyes of a mammalian subject in need of such treatment once a day.

(2) The state of the prior art

The state of prior art recognizes utility of some of 15-keto-prostaglandin compounds for the treatment of hypertension and glaucoma (See page 3, lines 15-19 of the instant specification). Especially the prior art recognizes the use of PGF2α derivatives as an ocular hypotensive agent that is useful for treatment of hypertension and glaucoma (See Jack DeRuiter, Principles of Drug Action, Fall 2002, Table in page 5, bottom of page 18 thru page 21).

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. Although the structure of prostaglandins are closely related to each other by their common prostanoic acid skeleton, the physiological activity of prostaglandins (i.e., PGA, PGB, PGC, PGD, PGE, PGF, PGG, PGH, PGI and PGJ) are considered to be vastly differed from each other depending upon substitution patterns in the cyclopentane ring and the side chains (See Jack DeRuiter, Principles of Drug Action, Fall 2002; US 3932389).

(5) The breadth of the claims

The claims are very broad due to the vast number of possible compounds of that are described as being "15-keto-prostaglandin compound having a ring structure at the end of the ω chain" or "15-keto-prostaglandin compound represented by formula (I)". The specification defines that "15-keto-prostaglandin compound" is meant any derivatives or analogs (including substituted derivatives) of a compound having an oxo group at 15-position of the prostanoic acid skeleton instead of the hydroxy group, irrespective of the configuration of the five-membered ring, the number of double bonds, presence or absence of a subsitutent. The scope of the instant claims encompasses 15-keto-PGAs, -PGBs, -PGCs, -PGDs, -PGEs, -PGFs, -PGGs, -PGHs, -PGIs or -PGJs and their derivatives.

(6) The amount of direction or guidance presented

As stated above, the specification discloses that some 15-keto-PG compounds have IOP reducing effects and are effective for treatment of ocular hypertension and

glaucoma (which has been incorporated by references US 5,001,153; US 5,151,444; US 5,166,178 and US 5,212,200). As the specific embodiment of the claimed invention, 13,14,dihydro-15-keto-17-phenoxy-18,19,20-trinor-PGF2α-isopropyl ester, 13,14,dihydro-15-keto-17-phenyl-18,19,20-trinor-PGF2α-isopropyl ester and 13,14,dihydro-15-keto-18-phenyl-19,20-dinor-PGF2α-isopropyl ester are disclosed as the compounds of the formula (I), and tested for their efficacy in lowering IOP in monkey (Figures 1-3).

However, the specification provides no guidance, in the way of enablement for the full scope of "15-keto-prostaglandin compound having a ring structure at the end of the ω chain " or "15-keto-prostaglandin compound represented by formula (I)" other than the 15-keto-PGF2α compound represented by the formula (I). The specification fails to provide sufficient information or guidance that all compounds (e.g., 15-keto-PGAs, -PGBs, -PGCs, -PGDs, -PGEs, -PGFs, -PGGs, -PGHs, -PGIs or -PGJs and their derivatives) that are potentially suitable for the invention work similarly as to the exemplified 15-keto- PGF2α. The numerous possible compounds that are potentially suitable for the instant invention are generally recognized in the art as having diverse physiological activities, and the skill artisan would have not known that which compounds of the claimed "15-keto-prostaglandin compound having a ring structure at the end of the ω chain " or "15-keto-prostaglandin compound represented by formula (I)" are capable of accomplishing the desired result of the claimed invention without undue amount of experimentation.

(7) The presence or absence of working examples

The instant specification discloses 13,14,dihydro-15-keto-17-phenoxy-18,19,20-trinor-PGF2α-isopropyl ester, 13,14,dihydro-15-keto-17-phenyl-18,19,20-trinor-PGF2α-isopropyl ester and 13,14,dihydro-15-keto-18-phenyl-19,20-dinor-PGF2α-isopropyl ester as working examples that are useful the claimed invention.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of "15-keto-prostaglandin compound having a ring structure at the end of the ω chain" or "15-keto-prostaglandin compound represented by formula (I), or a pharmaceutically acceptable derivative" that would be enabled in this specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

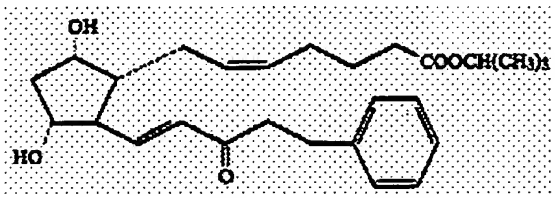
4. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Stjernschantz et al. (US 5296504).

Stjernschantz teaches the use of 15-dehydro-17-phenyl-18,19,20-trinor-PGF2α-isopropyl ester (Example 3 compound in Table I, column 14, lines 10-16) for lowering intraocular pressure, thereby, treating ocular hypertension and glaucoma (abstract;

column 1, lines 16-23; column 13, lines 24-30), wherein said compound is administered once or twice a day in the form of a pharmaceutical composition (column 5, lines 19-23).

Since the referenced compound "metes and bounds" the species of the genus or subgenus (claims 1-2), the reference anticipates the claimed invention.

The structure of 15-dehydro-17-phenyl-18,19,20-trinor-PGF2α-isopropyl ester is



Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

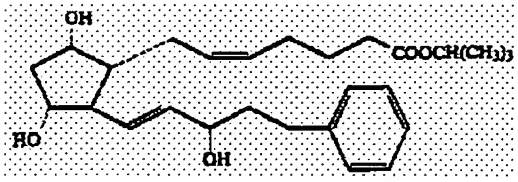
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

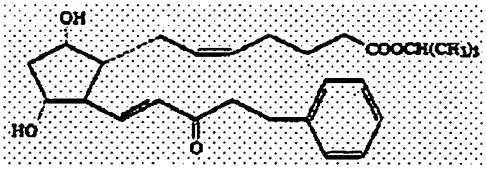
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stjernschantz et al. (US 5296504), and further in view of Ueno et al. (US 5,212,200).

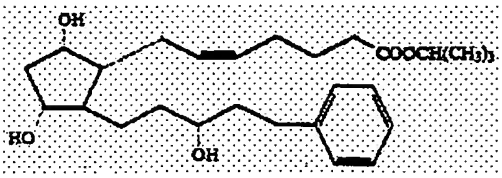
The teaching of Stjernschantz has been discussed in above 35 USC 102(b) rejection. Stjernschantz also teaches that modifying the omega chain and substituting a carbon atom in the chain with a ring structure exhibits an advantage over naturally occurring prostaglandins in that the irritating effect in the conjunctiva and cornea is considerably decreased or abolished (column 12, lines 16-21 and 27-31). As specific embodiments of the invention, Stjernschantz discloses PGF2α derivatives having ring structure such as phenyl or phenoxy at the end of the ω chain including 17-phenyl-18,19,20-trinor PGF2α-isopropyl ester, 16-phenoxy-17,18,19,20-tetranor-PGF2α-isopropyl ester, 18-phenyl-19,20-dinor-PGF2α-isopropyl ester and 13-14-dihydro-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester (having hydroxyl group at 15-position) in addition to the above mentioned 15-dehydro-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester (having oxo group at the 15-position). See column 4, lines 26-20 and TABLE I, III, IV and V (compounds 2, 4, 9 and 10).



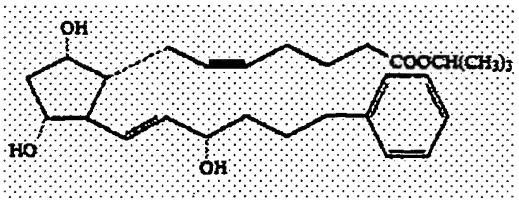
(17-phenyl-18,19,20-trinor PGF2α-isopropyl ester)



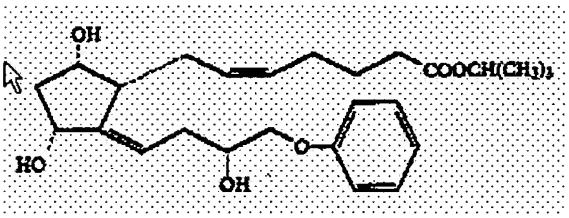
(15-dehydro-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester)



(13-14-dihydro-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester)



(18-phenyl-19,20-dinor-PGF2α-isopropyl ester)



(16-phenoxy-17,18,19,20-tetranor-PGF2α-isopropyl ester)

Ueno'200 teaches the use of 13,14-dihydro-15-keto-prostaglandins having a ring structure at the end of the ω chain (when Z is ring) for the treatment of ocular hypertension and glaucoma (column 4, lines 56-65; claims 2 and 3).

The teaching of Stjernschantz differs from the claimed invention in the use of 13,14-dihydro-15-keto-17-phenyl-18,19,20-trinor-prostaglandin compound or 13-14-dihydro-15-keto-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester. However, it would have been obvious to one having ordinary skill in the art at the time of the invention was made since the dehydrogenation of 15-hyrodxyl group to form 15-keto and the substitution of "CH2-CH2" with "CH=CH" at the 13-14 position would not significantly

alter the analogous properties of the compound of the reference due to close structural similarity of the compounds. One having ordinary skill in the art would have expected as taught by Stjernschantz (examples of 17-phenyl-18,19,20-trinor PGF2α-isopropyl ester and 15-dehydro-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester) that dehydration of 15-hydroxyl group to form 15-keto would not alter the analogous properties of the compound of the reference. Furthermore, One having ordinary skill in the art would have expected as taught by Stjernschantz (examples of 13-14-dihydro-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester, 17-phenyl-18,19,20-trinor PGF2α-isopropyl ester) that "CH2-CH2" with "CH=CH" at the 13-14 position would not alter the analogous properties of the compound of the reference. As evidenced by Ueno'200 that shows the activity of 13,14-dihydro-15-keto-prostaglandins (where the dehydrogenation of 15-hyrodxyl group to form 15-keto and the substitution of "CH2-CH2" with "CH=CH" at the 13-14 position) in treating ocular hypertension and glaucoma, one having ordinary skill in the art would have motivated to employ the claimed 13,14-dihydro-15-keto-17-phenyl-18,19,20-trinor-prostaglandin compound (i.e., 13-14-dihydro-15-keto-17-phenyl-18,19,20-trinor PGF2α-isopropyl ester) to treat ocular hypertension and glaucoma. One would have been motivated to combine these references and make the modification with the reasonable expectation of success because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-3 are rejected under the judicially created doctrine of double patenting over claims 2-19 of U. S. Patent No. 5,212,200 in view of Stjernschantz (US 5,296,504).

Although the conflicting claims are not identical, they are not patentably distinct from each other. Although the independent claim 2 or 3 of Ueno'200 alone does not specifically recite the claimed treatment of ocular hypertension and glaucoma, one having ordinary skill in the art would have known that the referenced compound that is useful for the treatment ocular hypertension or glaucoma would be useful the treatment of ocular hypertension and glaucoma. As evidenced by Stjernschantz (US 5,296,504), one having ordinary skill in the art would have expected that the agent that is useful for lowering IOP would be useful the treatment of ocular hypertension and/or glaucoma.

Although the claims of Ueno'200 does not specifically name "a ring structure at the end of the ω chain", ordinary skill in the art would have been able to "at once envisage" the claimed subgenus within the sufficiently limited or well delineated Z substituents (e.g., a straight-chain, a branched-chain or a ring) of generic chemical

formula of Ueno'220. Therefore, the referenced claims make obvious the instantly claimed composition.

Although the claims of the copending application is silent about the administration of said compound in "once a day" (required in the instant claims 1-3), however, those of ordinary skill in the art would have been readily optimized effective concurrent administration regimens as determined by good medical practice and the clinical condition of the individual patient. Determination of the appropriate administration frequency for the treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation.

7. Claims 1-4 are rejected under the judicially created doctrine of double patenting over claims 1-12 of U. S. Patent No. 6,458,836, and further in view of Stjernschantz et al. (US 5,296,504).

Although the conflicting claims are not identical, they are not patentably distinct from each other because: Both the instantly claimed subject matter and the copending application are drawn to a method for treating ocular hypertension and glaucoma comprising administering the 15-keto-prostaglandin compound, namely the compound represented by the formula (I), wherein the instantly claimed invention requires the "a ring structure at the end of the ω chain".

The scope of the present invention overlaps with the claims in US'086.

8. Claims 1-5 rejected under the judicially created doctrine of double patenting over claims 1-17 of U..S. Patent No. 6596765. Although the conflicting claims are not identical, they are not patentably distinct from each other. Although the referenced

method in claims 3-4, 9-14 and 17 differs from the instantly claimed method, one having ordinary skill in the art would have expected that the 13,14-dihydro-15-oxo-17-phenyl-18,19,20-trinor PGF2α N-ethylamide that is capable of maintaining a reduced intraocular pressure would be useful for the treatment of intraocular pressure. Furthermore, one having ordinary skill in the art would have expected that glaucoma that is an eye disorder characterized by increased intraocular pressure would be benefited from the referenced "maintaining a reduced intraocular pressure".

9. In looking in continuity data, it is noted that applicant has numerous issued patent and pending application encompassing the same or similar subject matter of the instant application. Applicant is aware of the patent and application is requested. Applicant review all subject matter considered same or similar, and submit the proper Terminal Disclaimer(s). For example, copending Application or patents 10/385621, US 5151444, US 5166178, US 6329426, US 5405846, US 5510383, US 5397797, US 5208256, US 5547968, US 5432174, US 5665773, US 5889052, US 5627209, US 6291521, US 6184250, US 6344478, US 6417228, US 6723748, US 6225348, US 6197821, US 5807892, US 6169111, US 6342524, US 5422369, US 5422368, US 5296504, US 5849791, US 6417230, US 6429226, US 6025392 and US 6160013 are considered to be same or similar subject matter(s). The examiner's time to write each and every rejection is extremely burdensome.

Conclusion

10. No Claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Primary Patent Examiner
AU 1614